Stem-ing the Tide of Disease

By Richard Schwab, MD, and Paul Cheng, MD, PhD

This year's ASH annual meeting had over 800 abstracts related to stem cells. Hematology has always been at the forefront of stem cell research, starting with the first non-syngeneic stem cell transplant in 1968. Many exciting advances in stem cell biology were presented and the growing number of pre-clinical and clinical applications of stem cell research is impressive.

Dr. Viviana Lo Cicero (abstract #282) presented work on the use of mesenchymal stem cells (MSC) in the treatment of acute renal failure. Using human cord blood, their group isolated MSC and grew them *ex vivo*. Then, using NOD-SCID mice, they induced acute renal failure with cisplatin. One day after this toxic insult, they infused the cultured human MSCs. After three additional days, blood urea nitrogen (BUN) levels and renal tubular degeneration were compared between treated and untreated mice. MSC infusion significantly reduced both BUN and renal tubular injury. Although the technical challenges of moving this approach into a clinical setting are daunting, this is an exciting demonstration of the potential of stem cell therapy.

In an oral session, Dr. Katarina Le Blanc will present abstract #753, the results of MSC infusion into patients with acute graft-versus-host disease (GVHD). Based on *in vitro* data for MSC inhibition of T-cell alloreactivity, their group has tested MSC infusion in 52 patients with steroid refractory GVHD. MSCs were obtained from HLA-identical siblings, haploidentical donors, and unrelated HLA-mismatched donors. Almost half of treated patients had a complete response along with nearly an additional quarter showing improvement. Additionally, no adverse side-effects were seen. While these data are preliminary, this certainly represents an encouraging step towards the use of MSC-based therapy.

In abstract #200, Dr. Alessandro Aiuti presented the results of stem cell gene therapy for ADA-SCID. At the San Raffeale Telethon Institute for Gene Therapy, their group has used retrovirally transfected autologous hematopoietic stem cells to treat children with ADA-SCID. With eight children treated and followed for a median of 3.1 years, no adverse events have been observed. Six children have been followed for at least one year and have progressively increasing lymphocyte counts. Most importantly, they have not had severe infections, and five of these children have very low levels of purine toxic metabolites. A recent publication from this group in the journal *Blood* described pre-clinical testing of an improved transduction system. Obviously, the ability to safely transduce hematopoetic stem cells *ex vivo* and reintroduce them into patients would have countless applications to permanently treat a host of diseases.

A very different, but equally exciting, pre-clinical result will be presented in abstract #728 by Dr. Frances Harding from Dr. Dan Kaufman's laboratory at the University of Minnesota. They are working on producing hematopoietic cells suitable for transfusion from human embryonic stem cells. They have developed a stirred culture system that improves cell yield four-fold and are studying the effect of environmental conditions on gene expression. With this system, they have found that short hypoxic exposure may maximize hypoxia-induced hematopoetic cell generation without causing hypoxia-induced cell death. Using embryonic stem cells to produce the blood products that are in such short supply is an exciting concept that appears to be achievable based on the presented research.